On the relation of dystonic movements to serum thyroxine levels

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Summary: A patient with psychomotor retardation secondary to delayed treatment of cretinism developed abnormal dystonic movements in the absence of other signs of toxicity during levothyroxine replacement therapy at a serum thyroxine level of 16 μg./100 ml. The dystonic movements disappeared when the serum thyroxine level fell. The abnormal movements were considered to be related to high thyroxine levels in this patient with pre-existing central nervous system dysfunction.

Résumé: Des mouvements involontaires choréoathétoïdes et dystoniques sont apparus chez une patiente arriérée atteinte de crétinisme alors que le niveau de thyroxine sérique était élevé. Ces mouvements sont disparus à des niveaux plus bas de thyroxine sérique. La présence de changements préexistant au niveau du système nerveux central a pu être un facteur prédisposant chez cette patiente.

Dystonic movements such as choreoathetosis[1,2] and spasmodic torticollis[3] may be presenting signs of thyrotoxicosis which gradually recede as thyroid function returns to normal.

Treatment with propranolol, a β-receptor blocker, has been shown to improve the dystonic, choreoathetoid and associated thyrotoxic manifestations before the laboratory values measuring thyroid function show a reduction towards normal.[1]

The purpose of this paper is to report dystonic movements of choreoathetoid, torsion spasm and opisthotonic types produced in a patient with hypothyroidism and psychomotor retardation, who was being treated with doses of levothyroxine exceeding the therapeutic range.

Case report

The patient, a girl aged 3 years and 4 months, first came to medical attention at 9 months of age because of severe psychomotor retardation. Labour had been induced three weeks before term because a sibling had died at birth. The delivery and perinatal course were unremarkable and she weighed 6 lb., 6 oz. at birth. Two siblings aged 8 and 11 years were healthy.

Examination showed many features of hypothyroidism. She had a peculiar facies with a broad, flat-tipped nose, large tongue, harsh low voice, carotenemic skin colour, marked pendular nystagmus, umbilical hernia and hypotonia. Height and weight were at the 25th percentile. There was obvious psychomotor retardation. Bone age was low, at a 3 months' level. There were slight irregularities of the epiphyseal ossification centres of the femurs. Thyroid function tests showed uniformly low values: thyroid trapping index was 0.81, 24-hour uptake 1.6%, T_3 resin uptake 24.6% and T_4 1.5 μg./100 ml. (normal range 4 to 11 μg./100 ml.). Thyroid scan (radiopertechnetate) was negative. A diagnosis of congenital nongoitrous hypothyroidism was made.

Levothyroxine was administered as outlined in Fig. 1. Only slight improvement occurred. The patient said a few words at 15 months and was trying to stand at that time. At 18 months she was hyperactive, with frequent periods of crying, irritability and increased appetite. Her pulse was recorded at between 120 and 140/min. and her reflexes were noted to be brisk at several examinations. Her serum thyroxine values were 14, 9.5 and 15 μg./100 ml. (therapeutic range: 4 to 12 μg./100 ml.) over a period of two years preceding the present illness.

At the age of 3 years and 1 month (September 1972) she became progressively more irritable and developed involuntary movements which at first consisted of episodic "winding" of the head. The serum level of thyroxine was 16 μg./100 ml. but the dosage of thyroxine was not decreased at that time because no obvious clinical signs of thyroid toxicity were present. Her movements progressively increased in frequency and 20 days later were nearly continuous. They involved the face, head and arms, and were mainly choreoathetoid in type. Grinding of the teeth and facial grimacing were also noted. Arching and twisting of the head and trunk along the longitudinal body axis resembled opisthotonic and torsion spasms. Her movements were increased by attempts at feeding, noise, or when she was upset. They remained nearly constant for 18 days except during sleep, when only infrequent myoclonic-like jerks were observed. She did not receive phenothiazines. Phenobarbital, given for 16 days, induced no changes in the movements described. Levels of serum glucose and electrolytes were normal. The EEG showed well developed alpha activity of 7 cycles per second with theta activity of 4 cycles per second intermingled. The abnormal movements had no electroencephalographic correlates. Skull x-rays and pneumoencephalogram were within normal limits. CSF examination showed no leukocytes; glucose level was 50 mg./100 ml. and protein 18 mg./100 ml.

After discontinuation of levothyroxine her movements rapidly became reduced and within 17 days disappeared completely. At this point TSH levels were elevated at 40 μu/ml. and did not rise further following injection of thyrotropin releasing factor. Her movements subse-

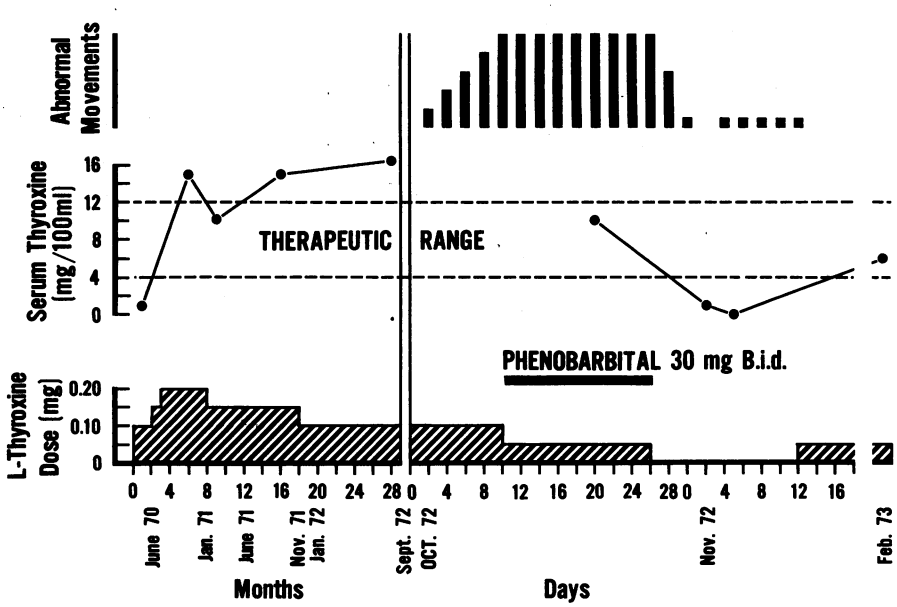

FIG. 1—Outline of the clinical course.

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quently remained absent at therapeutic blood levels of thyroxine (6 µg./100 ml.).

Discussion

This incapacitating, mainly dystonic disorder of movement developed on replacement therapy with levothyroxine producing serum levels of 14 to 16 µg./100 ml. The patient's symptoms disappeared after temporary discontinuation of thyroxine and remained absent on reduced dosage. It is considered that the movement disorder was related to high serum levels of thyroxine.

Brain-thyroid relationships are intriguing and incompletely understood. Thyroid hyperfunction increases excitability of the nervous system. It lowers the brain threshold for pharmacologically or electrically induced seizures in rats.[4] It is associated with emotional disturbances and induces a rapid, low amplitude tremor. Increased sensitivity of muscle synaptic membrane to transmitter substances in the presence of thyroid hormone can be demonstrated *in vitro*.[5] Thyroxine and triiodothyronine increase the excitability of spinal and cortical neurons, and increase the excitatory and inhibitory effects of glutamic acid and gamma-aminobutyric acid respectively, as studied iontophoretically in cats.[6] The enhancement of the effects of catecholamines by thyroxine is well known[7] and β-receptor blockade by propranolol is used to alleviate manifestations of thyrotoxicosis.[8] Administration of this drug led to the disappearance of the associated choreoathetosis in one case.[1]

The association of dystonia and choreoathetosis or torticollis with thyroid hyperfunction remains unexplained. In these cases pre-existing central nervous system structural changes cannot be excluded, but such changes are not suggested either by the history or the subsequent course. In the case reported here the structural changes associated with delayed treatment of cretinism, i.e. diminished neuronal size and immature axodendritic tree,[9] were probably complementary to the relatively mild iatrogenic hyperthyroid state in the production of the movements described.

Abnormal dystonic movements during thyroid replacement therapy should alert the physician to consider overtreatment as a cause. Pre-existing central nervous system abnormality, as in this case, may be a predisposing factor.

References

1. HEFFRON W, EATON PR: Thyrotoxicosis presenting as choreoathetosis. *Ann Intern Med* 73: 425, 1970
2. FIDLER SM, O'ROURKE RA, BUCHSBAUM HW: Choreoathetosis as a manifestation of thyrotoxicosis. *Neurology* 21: 55, 1971
3. GILBERT GJ: The medical treatment of spasmodic torticollis. *Arch Neurol* 27: 503, 1971
4. PASSOUANT-FONTAINE TH, FLANDRE C, PASSOUANT P: Influence de la thyroïde sur les crises convulsives provoquées chez le rat. *C R Soc Biol (Paris)* 149: 791, 1955
5. LAPLAUD J, GARGOUÏL YM: Modification de l'activité électrique de la fibre musculaire squelettique par l'acide triiodothyroacétique. *C R Soc Biol (Paris)* 154: 2361, 1960
6. DAVIDOFF RA, RUSKIN H: The effect of microelectrophoretically applied thyroid hormone on single cat central nervous system neuron. *Neurology* 22: 467, 1972
7. WALDSTEIN SS: Thyroid catecholamine interrelations. *Annu Rev Med* 17: 123, 1966
8. PIETRAS RJ, REAL MA, POTICHA GS, et al: Cardiovascular response in hyperthyroidism. *Arch Intern Med* 129: 426, 1972
9. EAYRS JT: Effects of thyroid hormones on brain differentiation, in *Brain-Thyroid Relationships,* edited by CAMERON MB and O'CONNER M, Ciba Foundation study group no 19, p 60, 1964

POSTGRADUATE COURSES

Doctors who attend refresher courses for which they pay tuition fees to a university, a teaching hospital or other educational institution in Canada may claim, as an income tax deduction, fees so paid if they exceed $25.00.

DERMATOLOGY IMMERSION COURSE. Toronto. December 1973 to April 1974. Each two-week course will include both training in a dermatology department in a teaching hospital and also in the private office of a staff dermatologist. Information: The Director, Division of Postgraduate Medical Education, Medical Sciences Building, University of Toronto, Toronto, Ont. M5S 1A8

JOURNEE D'ONCOLOGIE. Institut de Recherches Cliniques, Montréal. Le 29 mars 1974 (remise du 19 janvier). Renseignements: Directeur du Service d'éducation médicale continue, Université de Montréal, C.P. 6128, Montréal 101, Qué.

LES CERVICO-BRACHIALGIES. Hôpital Notre-Dame, Montréal. Le 26 janvier, 1974. Renseignements: Directeur du Service d'éducation médicale continue, Université de Montréal, C.P. 6128, Montréal 101, Qué.

NEONATAL HYPOGLYCEMIA. Ewart Angus Centre, McMaster University Medical Centre, Hamilton, Ont. January 30, 1974. Information: The Clinical Meetings Department, Wyeth Ltd., P.O. Box 370, Downsview, Ont. M3M 3A8

SEPTO-RHINOPLASTY. University of Toronto. February 3-8, 1974. Information: Director, Division of Postgraduate Medical Education, University of Toronto, Toronto, Ont. M5S 1A8

14TH ANNUAL REFRESHER COURSE FOR GENERAL SURGEONS. New Mount Sinai Hospital, Toronto. February 4-6, 1974. Information: Director, Division of Postgraduate Medical Education, University of Toronto, Toronto, Ont. M5S 1A8

OBSTETRIQUE-GYNECOLOGIE EN PRATIQUE GENERALE. Hôpital Saint-Luc, Montréal. Les 8-9 février 1974. Renseignements: Directeur du Service d'éducation médicale continue, Université de Montréal, C.P. 6128, Montréal 101, Qué.

REFRESHER COURSE FOR PRACTISING PATHOLOGISTS. University of Toronto. Febbruary 14-16, 1974. Information: Director, Division of Postgraduate Medical Education, University of Toronto, Toronto, Ont. M5S 1A8

REFRESHER COURSE IN PUBLIC HEALTH. Osler Hall, Academy of Medicine, Toronto. February 18-22, 1974. Information: Director, Division of Postgraduate Medical Education, University of Toronto, Toronto, Ont. M5S 1A8

PEDIATRICS, OBSTETRICS AND GYNECOLOGY. Regina General Hospital. February 21-23, 1974. Information: Mrs. M. P. Sarich, Continuing Medical Education, 408 Ellis Hall, Saskatoon, Sask. S7N 0W8

OFFICE GYNECOLOGY FOR FAMILY PRACTITIONERS. Ottawa Civic Hospital. February 21-22, 1974. Registration closes Feb. 1. Information: Department of Medical Education, Ottawa Civic Hospital, Ottawa, Ont. K1Y 4E9

SCIENTIFIC COMMUNICATIONS. Hospital for Sick Children, Toronto. March 18-20, 1974. Registration closes in mid-January. Information: Director, Division of Postgraduate Medical Education, University of Toronto, Toronto, Ont. M5S 1A8